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dopamine (DA) terminals in the basal ganglia of former capacitor workers. 248 subjects will undergo neuropsychological and neurological examinations, complete a comprehensive questionnaire, have blood drawn to measure serum PCB concentrations and undergo a noninvasive test to determine bone lead concentrations in Albany, New York. Approximately 40% of the subjects (chosen randomly) will be asked to undergo brain imaging at the Institute for Neurodegenerative Disorders in New Haven, CT to determine if PCBs reduce the number of basal ganglia DA terminals. IRB approvals have been obtained from all institutions; the X-ray fluoresence system (for bone lead measurement) has been assembled and calibrated; interview questionnaires have been piloted; a nurse/study coordinator has been hired and trained by staff epidemiologists and we have begun tracing, recruiting and testing subjects. To date twelve subjects are eligible (based on minimum age, distance of primary residence from Albany and the absence of certain medical conditions). Only three of them have refused to participate. Our goal is to schedule eight subjects per month until all 248 subjects have been tested.

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### INTRODUCTION

The major hypotheses to be tested in this project are that high-level occupational exposure to polychlorinated biphenyls (PCBs) will result in (i) decrements in performance on neuropsychological and neurological tests that reflect the historic PCB body burden of the individual and (ii) decrements that are correlated, perhaps causally, to reductions in the number of dopamine (DA) terminals in the basal ganglia of former 248 aging former capacitor workers who had previously been capacitor workers. employed at capacitor manufacturing facilities located approximately fifty miles north of Albany, NY will undergo neuropsychological and neurological examinations, complete a comprehensive questionnaire, have blood drawn to measure serum PCB concentrations, and undergo a non-invasive test to determine bone lead concentrations in Albany, NY. This latter measure is being collected to reduce the likelihood of a confound in the interpretation of which neurotoxicant (PCBs or lead) is responsible for the hypothesized deficits since some of the workers were also exposed to lead. Finally, 96 of these subjects (chosen on a random basis) will be asked to participate in the second portion of the study that will entail brain imaging using  $\beta$ -CIT SPECT to determine possible reductions in the number of basal ganglia DA terminals. Imaging will take place at the Institute for Neurodegenerative Disorders in New Haven, CT.

### **BODY**

In order to test the above hypotheses in this major epidemiological study, we have gathered a team of internationally recognized experts in the epidemiology of environmental and occupational exposure to PCBs, the neurology of movement disorders and Parkinson's Disease, the assessment of toxicant-induced deficits in neuropsychological function, measurement of serum PCB concentrations, non-invasive determination of bone lead concentrations, and brain imaging of central dopamine neurons and their relationship to movement disorders, including Parkinson's Disease.

The following narrative provides brief descriptions of the necessary—and time consuming—procedures we have carried out in the first year of the project that have laid the groundwork for a successful study that is currently underway.

### We Have Obtained Human IRB Approvals from All Member Institutions

Member institutions (and the investigators associated with each institution) include; the New York State Department of Health (Seegal, Fitzgerald), the University at Albany (McCaffrey, Haase), Albany Medical Center (Factor, Molho), the Institute for Neurodegenerative Disorders (Marek, Seibyl) and the Mount Sinai School of Medicine (Wolff, Todd). IRB approvals have been obtained from each of the above institutions as well as from the Surgeon General's IRB, as required by the U.S. Army Medical Research and Materiel Command. Because of the number of institutions involved, this has been a long and painstaking process that has been complicated by the decision to determine bone lead concentrations (see below).

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PCBs Alter Dopamine Mediated Function in Aging Workers

Seegal, Richard F.

### We Have Installed and Calibrated the K-Shell X-Ray Fluorescence System for Non-Invasive Measurement of Bone Lead

We deemed it necessary, after the initial application had been approved for funding, to control for potential confounding of our dependent variables due to the likelihood that many of the capacitor workers may have had prior occupational exposure to lead, either at the capacitor plants or at other work sites. Thus, we requested a modification of the original Statement of Work (SOW) and received a supplement to the original budget in order to set up a bone lead measurement system—one of only a handful in the United States. However, the need for the Food and Drug Administration (FDA) to review the use of the X-Ray Fluorescence system in humans prior to initiating the study (the detector contains a low level radioactive source) delayed our setting up the X-Ray Fluorescence system from May 2002 until late August 2002. A letter of that determination from the FDA is attached in Appendix 1.

Despite these delays, the X-Ray Fluorescence System has now been set up in a room remodeled solely for this study and the system has been initially calibrated by Dr. Andrew Todd of Mount Sinai School of Medicine. In addition he has trained several Albany staff in the procedures necessary for calibration and trouble shooting. We presently carry out a full calibration of the system using 'phantom' limbs (*i.e.*, plaster of paris casts doped with different concentrations of lead) twice weekly—a task that requires eight to ten hours to complete for each calibration. A summary of the installation, training of personnel and the results of calibration of the X-Ray Fluorescence System at the New York State Department of Health (NYSDOH) is provided in Appendix 2.

### We Have Assembled and Test-Piloted a Comprehensive Interview Form/Questionnaire

The interview form includes detailed questions on: the occupational history of the participant; their health status, including the use of prescription and over-the counter drugs, and reproductive history for women; their possible exposure to environmental neurotoxicants, either by living near point sources of contamination or due to recreational exposure to putative neurotoxicants; their consumption of high fat food products that may contain significant concentrations of PCBs; whether or not they caught and consumed contaminated fish from the Hudson River or the nearby Great Lakes; consumption of alcohol and caffeinated beverages and use of tobacco. This questionnaire takes approximately 1.5 to 2 hours to complete. Each subject is given the opportunity to meet with the study coordinator at a Public Health office near their homes and complete the questionnaire several days prior to traveling to Albany. A copy of the questionnaire is provided in Appendix 3.

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PCBs Alter Dopamine Mediated Function in Aging Workers

### We are Now Tracking, Screening, Recruiting and Testing Subjects

In collaboration with epidemiologists at the Center for Environmental Health (a division of the NYSDOH), who are co-investigators on this project, we have developed procedures for tracing, screening and determining the eligibility of prospective subjects. These procedures are described below in Appendix 4.

In addition, a copy of the informational materials sent to prospective participants is presented in Appendix 5. This packet also includes a letter of support from the executive council of the local electrical workers union that represented the former capacitor workers as well as a letter from a former union organizer who personally knows the principle investigator, Dr. Richard Seegal. These letters, we believe, are instrumental in convincing subjects to participate in the somewhat arduous tasks needed to adequately test the above hypotheses and reflect the level of effort and planning we have devoted to this project. Indeed, of the twelve subjects we have contacted to date, only three have refused to participate!

### Albany-based Investigators Meet on a Monthly Basis

In order to facilitate communication between these individuals who are located at the different institutions in Albany, we meet on a monthly basis to discuss any issues, including problems that arise, in the conduct of the study. These meetings have proven to be extremely useful and allow us to avoid many of the pitfalls that might otherwise occur in the conduct of this complicated multi-institutional epidemiological study. Topics discussed include: how to best report results to subjects' physicians if abnormal neurological and neuropsychological deficits are seen; issues of confidentiality and database development for reporting results for statistical analyses.

### KEY RESEARCH ACCOMPLISHMENTS

Because this is an epidemiological study—and one that is just getting underway—the key research accomplishments are those described in the above sections. As in all epidemiological studies, presentation of interim results prior to the collection of all data—without the entire data set and the accompanying statistical analyses to control for potential confounders—is at best misleading and at worse may result in conclusions that must be withdrawn following collection of the additional data.

### **REPORTABLE OUTCOMES**

As an invited presenter at the New York Academy of Sciences conference titled: "Parkinson's Disease: The Life Cycle of the Dopamine Neuron", I presented the overall design for this study and the background for the hypotheses to be tested. This conference held at the Doral Forrestal Conference Center in Princeton, NJ on September 18-20, 2002, was supported by the U.S. Army Medical Research and Materiel Command. The abstract and manuscript from that presentation are attached in Appendix 6.

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Seegal, Richard F.

### **CONCLUSIONS**

I have had the most experience conducting laboratory studies, including *in vitro* studies, where results are publishable as soon as the researcher has replicated the findings. As discussed in the above section 'Key Research Accomplishments', this is not the case for epidemiological studies that most often require several years of effort before all subjects have been tested and results are statistically analyzed. This, however, is not an excuse for the lack of reportable products at this time—indeed, given the complexity of the project (*i.e.*, the diverse dependent variables that are being collected; the number of investigators and member institutions) we have made considerable progress in producing the instruments (both paper and scientific) necessary for successfully carrying out the study.

### **APPENDICES**

**Appendix 1:** Letter of determination from FDA's review of human use of the X-ray fluorescence (XRF) system for non-invasive measurement of bone lead.

Appendix 2: XRF progress report prepared by Dr. Andrew Todd.

Appendix 3: Study interview form/questionnaire.

Appendix 4: Flow chart for tracing, screening and recruiting procedures for study subjects.

Appendix 5: Informational material sent to prospective study participants.

**Appendix 6:** Abstract and manuscript from presentation at New York Academy of Sciences conference titled: "Parkinson's Disease: The Life Cycle of the Dopamine Neuron", Princeton, NJ, September 18-20, 2002.

Neurological Effects of Polychlorinated Biphenyls – Does Occupational Exposure Alter Dopamine-Mediated Function? R.F. Seegal<sup>1,4</sup>, K. Marek<sup>2</sup>, S. Factor<sup>3</sup>, R. McCaffrey<sup>4</sup>, R. Haase<sup>4</sup> and M. Wolff<sup>5</sup>. <sup>1</sup>Wadsworth Center, New York State Dept. of Health, Albany, NY; <sup>2</sup>Institute for Neurodegenerative Disorders, New Haven, CT; <sup>3</sup>Albany Medical Center, Albany, NY; <sup>4</sup>University at Albany, Albany, NY and <sup>5</sup>Mount Sinai School of Medicine, New York, NY.

Seegal, R. F. Neurological Effects of Polychlorinated Biphenyls – Does Occupational Exposure Alter Dopamine-mediated Function? *In*: Parkinson's Disease: The Life Cycle of the Dopamine Neuron, Annals of the New York Academy of Sciences, in press.

### **APPENDIX 1**

Letter of determination from FDA's review of human use of the X-ray fluorescence (XRF) system for non-invasive measurement of bone lead



Food and Drug Administration 9200 Corporate Boulevard Rockville MD 20850

AUG 2 7 2002

Richard F. Seegal, Ph.D. Wadsworth Center New York State Department of Health Empire State Plaza Albany, New York 12201-0509

Re: Human Bone Lead Measurements by X-Ray Fluorescence (XRF)

Dear Dr. Seegal:

The Food and Drug Administration (FDA) has reviewed the information you provided by e-mail dated June 17, 2002. The information describes an instrument and method, referenced above, for non-invasively obtaining an estimate of the concentration of lead in bone. Based on the description provided and comparison to a device that had previously been marketed for this use, we have determined that the device provides a radiation dose one-quarter the dose of the previously marketed device. Therefore, when used in the described manner, we have determined that your device poses a non-significant risk to human subjects.

Additionally, you indicate that the device will not be used for diagnostic purposes but instead will be used to provide a means to statistically control for a potential confounder in an epidemiological study. Because your research is not designed to investigate the safety and effectiveness of the device and the device will be used as a research tool, your research is outside the scope of the investigational device exemption (IDE) regulation (see 21 CFR 812.2(a), available on the internet at

http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/showCFR.cfm?CFRPart=812). Therefore, your research is not subject to the requirements of the IDE regulation; however, you should still obtain institutional review board approval and informed consent for your study.

If you have any questions regarding the risk determination for the device, please contact Robert A. Phillips, Ph.D. at (301) 594-1212 x 130. Questions regarding the IDE regulation may be directed to Marsha Melvin at (301) 594-1190 x 107.

Sincerely yours,

Nancy C. Brogdon

Director, Division of Reproductive,

Abdominal, and Radiological Devices

Office of Device Evaluation

Center for Devices and Radiological Health

### **APPENDIX 2**

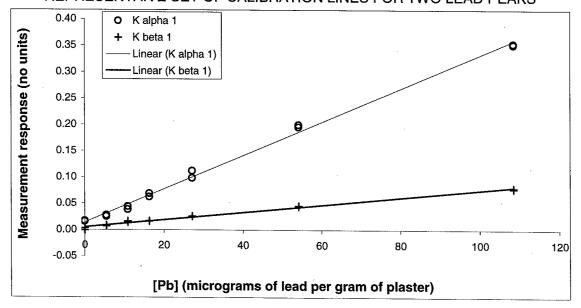
X-ray fluorescence system progress report prepared by Dr. Andrew Todd

The tasks of the subcontract consist of the purchase, construction and calibration of a bone lead measurement system for use by NYSDOH; training of the bone lead measurement system operator in Albany; and analysis of the raw data (in electronic form) generated with the bone lead measurement system.

Dr. Todd has supervised and overseen most aspects of the X-ray Fluorescence measurement system for the *in vivo* measurement of lead in bone. The bone lead measurement system was first constructed at Mount Sinai and calibrated, ensuring delivery of an operational system and providing reference calibration information. The measurement system was then disassembled and moved to the Wadsworth Laboratories where it was reassembled and tested. Once functional, the measurement system was optimized with regard to operational parameters of the spectroscopy electronics (e.g., peak shaping rise time and flat-top).

Dr. Todd trained Mr. Brosch and Dr. Parsons in both the calibration and *in vivo* use of the bone lead measurement system. Initial calibration was then performed on-site and the acquired spectra (distributions of scattered and fluorescent photons) were sent to Mount Sinai for analysis. This analysis required (as it always done) tuning to the particulars of the spectroscopy electronics and Dr. Todd fulfilled these needs. As expected, the analysis of the acquired spectra revealed minor instability in the measurement system in the earliest days, but this instability disappeared as the measurement system electronics 'settled', again, as expected. Twelve complete calibration lines have been obtained: each calibration line consists of two measurements of each of seven lead-doped plaster-of-Paris calibration standards that encompass a concentration range from a nominal blank to  $107 \mu g/g$  plaster-of-Paris (which is substantially greater than the concentrations expected from the study population). Dr. Todd also provided some input to the selection of the bone lead measurement system operator.

### REPRESENTAIVE SET OF CALIBRATION LINES FOR TWO LEAD PEAKS



One of the twelve pairs of Pb K $\alpha$ 1 (upper line) and K $\beta$ 1 (lower line) calibration lines obtained with the bone lead measurement system.

### **APPENDIX 3**

Study interview form/questionnaire

# DO PCBs ALTER DOPAMINE MEDIATED FUNCTION IN AGING WORKERS INTERVIEW FORM?

Participant ID: [#1	#2 #3 #4 #5 #6	#7_]	Interviewer:	ver:		Date of Interview:	rview://
First Name:	Last Name:				Gender:	1. Male	2. Female
CORRECTIONS: F	First Name:		Last Name:				
Mailing Address:	Street:						
	City:	St	State:	Zip:		,	
	Home Phone: ( )	W	Work Phone: (	(			
CORRECTIONS: Mailing Address:	Street:						
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Date of Birth:					,		
Height: (without shoes)	Ft.	_ In.				·	
Weight: (with indoor clothing)	othing)lbs.	.8					
Years of school completed:	ed:						
Current marital status:	1. Never Married	2. Married 3.	3. Widowed	4. Divorced	5. Separated	6. Live-in-Partner	tner
Name of current spouse/partner:	partner: First Name:			Last Name:			

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### RESIDENCE HISTORY

ID: [ #1 #2 #3 #4 #5 #6 #7]

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years you lived at each address. Please include second homes if you spent a total of 90 or more days per year there. Were any of the homes you lived in for the past 25 years located in the same building with or within a 5 minute walk of commercial or industrial establishments? The business must have been there when you lived in that house. Starting with your present residence and working backwards for the past 25 years, please indicate every residence you have lived at for one year or more and the number of

							7
						1= Building	
Residence	From	To		Address	Type of Establishment	2= Within 5	
	Year	Year				Min. Walk	
					1= Yes 2= No 8= No Response 9= Don't Know	(circle ans)	Т
					Is this this home in the same building or on the same block (i.e.,		
					within a 5 minute walk) as any commercial or industrial		
					establishment? 1. Yes 2. No		
RI		Current			Beauty Salon 1 2 8 9	1 2	
Current		Year			Dry Cleaners 1 2 8 9	1 2	
Residence			City:		Gas Station, service station, or autobody shops 1 2 8 9	1 2	
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			State.	. Zin.	Print shops or photo processing shops 1 2 8 9	1 2	
,					Carpentry or furniture repair or refinishing shops 1 2 8 9	1 2	_
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<b>E</b> 2					the same block (i.e., within a 5 minute walk) as any commercial or		
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					Other (specify): 1 2 8 9	1 2	
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1. Yes					Dry Cleaners 1 2 8 9	1 2	
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RESIDENCE HISTORY (continued)	CE HIST	ORY (coi	ntinued)	ID: [ #1 #2 #3 #4 #5	[ 2# 9#
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2. No			City:	service station, or autobody shops 1 2	1 1 2
8. NR				1 2 8	1 2
Months:			State: Zip:		1 1 2 2
				. 1 2 8	1 2
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1. Yes				1 2 8	1 2
2. No NB			City:	∞ ∞	1 - 2 2 2
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				Carpentry or furniture repair or refinishing shops 1 2 8 9 Other (specify):	1 2 2
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SSIDENCE HISTORY (conti	
CE	

ID: [#1 #2 #3 #4 #5 #6 #7]

Residence	From	To	Address	Type of Establishment	1= Building 2= Within 5
	Year	Year		1= Yes 2= No 8= No Response 9= Don't Know	Min. Walk (circle ans)
R10 Second Home? 1. Yes 2. No 8. NR Months:	·		City:	When you lived there, was this home in the same building or on the same block (i.e., within a 5 minute walk) as any commercial or industrial establishment?  1. Yes 2. No  Beauty Salon  Dry Cleaners  Gas Station, service station, or autobody shops Factories or Mills (specify):  Carpentry or furniture repair or refinishing shops Other (specify):  1. 2 8 9  Carpentry or furniture repair or refinishing shops Other (specify):	1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1
R11 Second Home? 1. Yes 2. No 8. NR Months:			City:	When you lived there, was this home in the same building or on the same block (i.e., within a 5 minute walk) as any commercial or industrial establishment?  1. Yes 2. No  1 2 8 9  Dry Cleaners  Gas Station, service station, or autobody shops  Factories or Mills (specify):  1 2 8 9  Print shops or photo processing shops  Carpentry or furniture repair or refinishing shops  Other (specify):  1 2 8 9	222222
R12 Second Home? 1. Yes 2. No 8. NR Months:			City:	When you lived there, was this home in the same building or on the same block (i.e., within a 5 minute walk) as any commercial or industrial establishment?  1. Yes 2. No  Beauty Salon  Dry Cleaners  Gas Station, service station, or autobody shops  Factories or Mills (specify):  Print shops or photo processing shops  Carpentry or furniture repair or refinishing shops  Other (specify):  1 2 8 9  Other (specify):  1 2 8 9	2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2

RESIDENCE HISTORY (continued)	E HIST	ORY (co	ntinued)	ID: [ #1 #2 #3 #4 #5	[
Residence	From	To Year	Address	Type of Establishment	1= Building 2= Within 5 Min. Walk
				1= Yes 2= No 8= No Response 9= Don't Know	(circle ans)
R13				When you lived there, was this home in the same building or on the same block (i.e., within a 5 minute walk) as any commercial or industrial ortabilishment?	
Home?				2.100 1 2 8	1 2
1. Yes				1 2 8	$\frac{1}{1}$ $\frac{2}{2}$
2. No			City:	or autobody shops 1 2 8	1 2
8. NR			Chata		1 1 2 2
Months:				thing shops 1 2 8	1 - 2 2
					7
R14 Second				When you lived there, was this home in the same building or on the same block (i.e., within a 5 minute walk) as any commercial or industrial establishment?	
Home?				1	1 2
1. Yes				∞	1 2
2. No			City:	or autobody shops 1 2 8	1 2
8. NR				1 2 8	1 2
Months:			State: Zip:	1 2 8	1 2
				Carpentry or furniture repair or refinishing shops 1 2 8 9 Other (specify): 1 2 8 9	1 2 2
				When you lived there was this home in the same building or on	
R15				the same block (i.e., within a 5 minute walk) as any commercial or	
Second				industrial establishment? 1. Yes 2. No	
Home?				∞	1 2
1. Yes				1 2 8	1 2
2. No			City:	or autobody shops 1 2 8	1 2
8. NR				1 2 8	1 2
Months:			State: Zip:	1 2 8	1 2
				Carpentry or furniture repair or refinishing shops 1 2 8 9	7 .
				$\circ$	1 2

## OCCUPATIONAL HISTORY.

ID: [ #1 #2 #3 #4 #5 #6 #7

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Are you retired? 1. Yes 2. No

8. NR

If yes: In what year did you retire?

Have you worked outside the home on a volunteer basis?

1. Yes 2. No 8. NR

Starting with your most recent volunteer job, please indicate the two most recent volunteer jobs that you have held. Also indicate if you were exposed to any chemicals or other substances while volunteering and the frequency of exposure. [HAND SUBJECT CHEMICAL LIST]

	Datos				If yes list name of chemical(s)
	From To (Mo/Yr)	To Mo/Yr)		Exp	and frequency of exposure.
	(11 (11)				1=<1/week 2=<1/day 3=daily
Most					
Recent			Organization Name City State	1. Yes	
	Hours per Week	Week	Time of Organization.	,	1 2 3
î —	Circle 01	ne: -20	Type of Organization.	7. No	
	21-30 31-40	140	Description of work:	8. NR	
	40+	_			
				9. DK	
-			Job Title:		
6		_			
ì			Organization Name City State	1. Yes	
-	Hours per Week	Week			
	Circle on	e:	Type of organization:	2. No	
	21-30 31-40	-20	Description of work:	e V	1 2 3
	40+	}		9. NK	
				9. DK	
		,	Job Title:		

Now starting with your most recent paid job and working backwards, please indicate every job that you have held for three months or more at GE or for one year or more elsewhere. Also indicate if you were exposed to any chemicals or other substances on the job and the frequency of exposure.

OCCUP	ATIONAL	HISTOR	OCCUPATIONAL HISTORY (continued)	ID: [#1	#2	#3 #4 #5 #6 #7]
	Prom [Mo/Yr] (I	es To (Mo/Yr)	Description	ption	Exp	If yes, list name of chemical(s) and frequency of use.  1=<1/week 2=<1/day 3=daily
Most Recent 1)		/— — /— —/—  Hours per Week Circle one: <10 11-20 11-31 31-40 40+	Company Name  Type of industry:  Description of work:  Job Title:	State	1. Yes 2. No 8. NR 9. DK	1 1 2 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3
2)	Hours per Week Circle one: <10 11-20 21-31 31-40 40+	/	Company Name Type of industry:  Description of work:  Job Title:	State	1. Yes 2. No 8. NR 9. DK	1 2 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3
3)	Hours per Week Circle one: <10 11-20 21-30 31-40	r Week: 0ne: 11-20	Company Name  Type of industry:  Description of work:  Job Title:	State	1. Yes 2. No 8. NR 9. DK	1 2 3 3 1 5 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3

OCCUP	OCCUPATIONAL HISTORY (continued)	STORY	Y (continued)	ID: [#1	1 #2	#3 #4 #5 #6 #7]
	Dates From To (Mo/Yr) (Mo/Yr)	To Io/Yr)	Description		Ехр	If yes, list name of chemical(s) and frequency of use. 1=<1/week 2=<1/day 3=daily
(7)	Hours per Week Circle one: <10 11-20 21-32 31-40 40+	/ : : : : : : : : : : : : : : : : : : :	Company Name  Type of industry:  Description of work:  Job Title:	State	1. Yes 2. No 8. NR 9. DK	1 1 2 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3
5)	Hours per Week Circle one: <10 11-20 21-32 31-40 40+		Company Name  Type of industry:  Description of work:  Job Title:	State	1. Yes 2. No 8. NR 9. DK	1 1 1 1 1 5 5 3 3 3 3 3 3 3 3 3 3 3 3 3
(9	Hours per Week Circle one: <10 11-20 21-31 31-40		Company Name  Type of industry:  Description of work:  Job Title:	State	1. Yes 2. No 8. NR 9. DK	1 1 1 1 2 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3

1 #2 #3 #4 #5 #6 #7 ]	Exp   If yes, list name of chemical(s) and frequency of use.   1=<1/week 2=<1/day 3=daily	1. Yes 1. 2 3 2. No 1. 2 3 8. NR 1. 2 3 9. DK 1. 2 3 9. DK	1. Yes  2. No  8. NR  9. DK	1. Yes  2. No  8. NR  9. DK
D: [#1		State	State	State
	Description	City	City	City
Y (continued)		Company Name Type of industry: Description of work: Job Title:	Company Name Type of industry: Description of work:	Company Name Type of industry:  Description of work:
OCCUPATIONAL HISTORY (continued)	Dates From To (Mo/Yr) (Mo/Yr)	/	/  / Hours per Week Circle one: <10 11-20 21-33 31-40 40+	/
OCCUPA	,	C	8	(6

## OCCUPATIONAL HISTORY OF SPOUSE/ LIVE-IN-PARTNER

ID: [ #1 #2 #3 #4 #5 #6 #7 ]

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Now I need to ask you about the occupational history of your current and/or past spouses or live-in-partners.

How many times have you been married or had a live-in-partner?

Please start with the most recent and work backwards

	Current or Most Recent Spouse/Partner	Previous # 1 Spouse or Partner	Previous # 2 Spouse or Partner	Previous # 3 Spouse or Partner
During the time that you lived together, did he or she work at the GE plants located in Fort Edward or Hudson Falls?	1.Yes 2.No 8.NR 9.DK  If Yes: When? (Year)  StartedEnded  StartedEnded  What type of work did he or she do?	1.Yes 2.No 8.NR 9.DK  If Yes: When? (Year)  StartedEnded  StartedEnded  What type of work did he or she do?	1.Yes 2.No 8.NR 9.DK  If Yes: When? (Year)  StartedEnded  StartedEnded  What type of work did he or she do?	1.Yes 2.No 8.NR 9.DK  If Yes: When? (Year)  StartedEnded  StartedEnded  What type of work did he or she do?
During the time that you lived together, did he or she work in any other job that involved the manufacturing, processing or servicing of transformers, capacitors, or other electrical equipment?	1.Yes 2.No 8.NR 9.DK  If Yes: When? (Year) StartedEnded StartedEnded What type of work did he or she do?	1.Yes 2.No 8.NR 9.DK  If Yes: When? (Year)  Started Ended  Started Ended  What type of work did he or she do?	1.Yes 2.No 8.NR 9.DK  If Yes: When? (Year)  StartedEnded  StartedEnded  What type of work did he or she do?	1.Yes 2.No 8.NR 9.DK  If Yes: When? (Year)  StartedEnded  StartedEnded  What type of work did he or she do?
During the time that you lived together, did he or she work in any other job that involved exposure to PCBs?	1.Yes 2.No 8.NR 9.DK  If Yes: When? (Year)  Started Ended Started Ended do?	1.Yes 2.No 8.NR 9.DK  If Yes: When? (Year)  StartedEnded  StartedEnded  What type of work did he or she do?	1.Yes 2.No 8.NR 9.DK  If Yes: When? (Year)  StartedEnded  StartedEnded  What type of work did he or she do?	1.Yes 2.No 8.NR 9.DK  If Yes: When? (Year)  StartedEnded  StartedEnded  What type of work did he or she do?

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ID: [ #1 #2 #3 #4 #5 #6 #7 ]

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Now I'd like to ask you about some of your usual food habits in the past year.

		Av	Average Consumption	umption			
	Never/					Has this	
Dairy	< once a	1-4/	2-6/	1 - 37	<b>4+</b> /	changed in the	1 = incr
	month	month	week	day	day	last 2 years?	2 = decr
Skim/Low Fat							
Milk (8 oz)							
Whole							
Skim/Low Fat		-					
Yogurt (8 oz)							
Whole							
Skim/Low Fat							
Ice Cream (1/2 cup)							
Whole							,
Soft Cheeses: (Cottage or ricotta							
cheese; 1/2 cup)							
Hard Cheeses: (American, cheddar-							
plain or as part of a dish; 1 slice or 1					-		
oz)							
Butter, added to food or bread, or		, .					
used in cooking (1 teaspoon)							
Eggs (1)					. 10		

Dietary History: (continued)	•	·		D: [	ID: [ #1 #2 #3	#3 #4 #5 #6 #7	9 #1
		Ą	Average Consumption	sumption	٠		
Beverages	Never / < once a month	1 – 4 / month	2-6/ week	1 – 3 / day	4+ / day	Has this Changed in the last 2 years?	1 = incr $2 = decr$
Soda or other carbonated drink w/ Caffeine (12 oz.) (e.g. coke, diet coke, etc.)							
Tea (8 oz.) – not herbal							
Coffee (8 oz.) – not decaffeinated							
Animal Meats (4 - 6 oz.)	Never / < once a month	1 – 4 /month	2 – 6 /week	1 – 3 /day	4+ /day	Has this Changed in the last 2 years?	1 = incr $2 = decr$
Chicken or turkey							
Beef, pork, or lamb; including as a sandwich or mixed dish, e.g. stews, hamburger, casserole, lasagna, etc.				-			
Processed Meats (luncheon meats) (1 sandwich)							
Organ Meats (4 – 6 oz.)	Never / < once a month	1 – 4 /month	2 – 6 /week	1 – 3 /day	4+ /day	Has this Changed in the last 2 years?	1 = incr $2 = decr$
Liver							
Other organ meats: heart, brain, kidneys, tongue, tripe or stomach							

Dietary History: (continued)		ID: [#1	ID: [ #1 #2 #3 #4 #5 #6 #7 ]	9# 5#	#7_]
Fish from Supermarkets, Fish Stores and Restaurants	rants				
			Time Period		In the past year,
		Frequency	From Year Y		when was your last fish meal?
Have you eaten <b>fresh water fish</b> in the past <b>25</b> years?	1.Yes 2.No 8.NR 9.DK	Per Wk Mo Yr 25 Yr			
Have you eaten shark in the past 25 years?	1.Yes 2.No 8.NR 9.DK	Per Wk Mo Yr 25 Yr			
Have you eaten swordfish in the past 25 years?	1.Yes 2.No 8.NR 9.DK	Per Wk Mo Yr 25 Yr	·		
Have you eaten tuna steaks (or canned tuna) in the past 25 years?	1.Yes 2.No 8.NR 9.DK	Per Wk Mo Yr 25 Yr			

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id you trim the fat and skin from the fish $p$
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# Years Eaten:

# Years Eaten:

# Years Eaten:

South of the dam, Housatonic River,

Rt. 9 bridge to Troy dam,

other PCB contaminated waters)

Location:

Trim

Trim

Trim

Fry,

Fry.

Fry.

DIETARY HISTORY: Fresh Water Fish (continued)	(continued)	ID: [ #1 #2 #3	2 #3 #4 #5 #6 #7 ]
	If yes: Averag	If yes: Average number of meals/week, month, year and location	and location
Type of Fish	1993 or Before	1994 – Last Year	In the Past Year
	Amount	Amount	Amount
Fish # 3			
Type:	Year: From:To:		
(Location: North West of Glens Falls,	Per Wk Mo Yr	Per Wk Mo Yr	Per Wk Mo Yr
South of the dam, Housatonic River, other PCB contaminated waters)	# Years Eaten:	# Years Eaten:	# Years Eaten:
Location:	Fry	FryTrim	Fry
NR DK			
Fish # 4			
Type:	Year: From: To:		
(Location: North West of Glens Falls,	Per Wk Mo Yr	Per Wk Mo Yr	Per Wk Mo Yr
South of the dam, Housatonic River, other PCB contaminated waters)	# Years Eaten:	# Years Eaten:	# Years Eaten:
Location:	Fry	Fry	Fry
NR DK			

**Trim** = Did you trim the fat and skin from the fish prior to cooking?

DIETARY HISTORY: Fresh Water Fish (continued)	(continued)	D: [#1 #2	2 #3 #4 #5 #6 #7]
	If yes: Averag	Hyes: Average number of meals/week, month, year and location	r and location
Type of Fish	1993 or Before Amount	1994 – Last Year Amount	In the Past Year Amount
Fish # 5	,		
Type:	Year: From: To:		
(Location: North West of Glens Falls,	Per Wk Mo Yr	Per Wk Mo Yr	Per Wk Mo Yr
No. 2 of the Gam, Housatonic River, South of the dam, Housatonic River, other PCB contaminated waters)	# Years Eaten:	# Years Eaten:	# Years Eaten:
Location:	Fry	Fry	Fry
NR DK			
Fish # 6			
Type:	Year: From: To:		
(Location: North West of Glens Falls,	Per Wk Mo Yr	Per Wk Mo Yr	Per Wk Mo Yr
Kt. 9 bridge to 1 roy dam, South of the dam, Housatonic River, other PCB contaminated waters)	# Years Eaten:	# Years Eaten:	# Years Eaten:
Location:	FryTrim	Fry	Fry
NR DK			

**Trim =** Did you trim the fat and skin from the fish prior to cooking?

DIETARY HISTORY: Fresh Water Fish (continued)

ID: [#1 #2 #3 #4 #5 #6 #7]

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	H ves: Averag	Hves: Average number of meals/week, month, year and location	ır and location
Type of Fish	1993 or Before	1994 – Last Year	In the Past Year
	Amount	Amount	Amount
Fish # 7			
Type:	Year: From: To:		
(Location: North West of Glens Falls,	Per Wk Mo Yr	Per Wk Mo Yr	Per Wk Mo Yr
Kt. 9 bridge to 110y dain, South of the dam, Housatonic River, other PCB contaminated waters)	# Years Eaten:	# Years Eaten:	# Years Eaten:
Location:	Fry	Fry Trim	Fry
NR DK			
Fish # 8			
Type:	Year: From: To:		
(Location: North West of Glens Falls,	Per Wk Mo Yr	Per Wk Mo Yr	Per Wk Mo Yr
Kt. 9 bridge to 1 roy dain, South of the dam, Housatonic River, other PCB contaminated waters)	# Years Eaten:	# Years Eaten:	# Years Eaten:
Location:	Fry	Fry Trim	FryTrim
NR DK			

Trim = Did you trim the fat and skin from the fish *prior* to cooking?

[#1 #2 #3 #4 #5 #6 #7]	
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DIETARY HISTORY: Fresh Water Fish (continued)	

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	If yes: Average	If yes: Average number of meals/week, month, year and location	r and location
Type of Fish	1993 or Before	1994 – Last Year	
	Amount	Amount	Amount
Fish # 9			
Type:	Year: From: To:		
(Location: North West of Glens Falls,	Per Wk Mo Yr	Per Wk Mo Yr	Per Wk Mo Yr
South of the dam, Housatonic River, other PCB contaminated waters)	# Years Eaten:	# Years Eaten:	# Years Eaten:
Location:	Fry Trim	Fry	Fry
NR DK			
Fish # 10			
Type:	Year: From: To:		
(Location: North West of Glens Falls,	Per Wk Mo Yr	Per Wk Mo Yr	Per Wk Mo Yr
South of the dam, Housatonic River, other PCB contaminated waters)	# Years Eaten:	# Years Eaten:	# Years Eaten:
Location:	FryT	Fry Trim	Fry
NR DK			

**Trim** = Did you trim the fat and skin from the fish prior to cooking?

4,1 In the Past Year Per Wk Mo Yr 9# Per Wk Mo Yr Amount #2 # Years Eaten: # Years Eaten: #7 If yes: Average number of meals/week, month, year and location #3 Trim Fry # ID: [#1 1994 - Last Year Amount Per Wk Mo Yr Per Wk Mo Yr # Years Eaten: # Years Eaten: Trim Fry. 1993 or Before To: To: Amount Per Wk Mo Yr Per Wk Mo Yr # Years Eaten: \_ # Years Eaten: Year: From: \_ Year: From: DIETARY HISTORY: Fresh Water Fish (continued) Trim Fry. (Location: North West of Glens Falls, (Location: North West of Glens Falls, South of the dam, Housatonic River, South of the dam, Housatonic River, other PCB contaminated waters) other PCB contaminated waters) Type of Fish Rt. 9 bridge to Troy dam, Rt. 9 bridge to Troy dam, DK Fish # 11 Fish # 12 Location: Type: Type: R

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**Trim** = Did you trim the fat and skin from the fish prior to cooking?

Trim

Trim

Fry\_ Trim\_

Location:

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Fry

DIETARY HISTORY: Wild Game, Turtle	e, Turtle					H	ID: [ #1 #2 #3 #4 #5	#2 #	13 #4	#2	<b>L#</b> 9#	#7_1
Have you eaten bear in the last 25 years?		1) Yes	2) No	8) NR	9) DK							
Have you eaten wild duck in the last 25 years?	/ears?	1) Yes	2) No	8) NR	9) DK							
Have you eaten wild goose in the last 25 years?	years?	1) Yes	2) No	8) NR	9) DK							
Have you eaten turtle in the last 25 years?		1) Yes	2) No	8) NR	9) DK							
	If yes	If yes to any of al	hove: Ave	rage numb	er of meals	of above: Average number of meals per week, month, year or 25 year period and location	nonth, year	or 25 ye.	ar perio	d and lo	cation	
Type of Wild Game		Pa	Past Year			10.00		Past 2	Past 25 Years	·		
	Years:					Years:						
Type:		,										<b> </b>
Location:												· ·
	Per V	Per Wk Mo Yr					Per Wk Mo Yr 25 Yr	Mo Yr	25 Yr		,	
NR DK	Fry	Trim				Fry	_ Trim.	e E	1			
Type:	Years:					Years:						i
Location:												ı
	Per W	Per Wk Mo Yr					Per Wk Mo Yr	Mo Yr	25 Yr			
NR DK									,			
	Fry	Trim			,	Fry	Trim.	m				

Fry = Did you cook the game by frying it?

Trim = Did you remove the fat and skin from the game prior to cooking?

DIETARY HISTORY: Wild Game (continued)	(continued)	ID: [ #1 #2 #3 #4 #5 #6 #7 ]
	If yes: Average number of meals per week, month, year or 25 year period	or 25 year period
Type of Wild Game	Past Year	Past 25 Years
Type:	Years:	Years:
Location:	Per Wk Mo Yr	Per Wk Mo Yr 25 Yr
NR DK	Fry Trim	Fry Trim
Type:	Years:	Years:
Location:	Per Wk Mo Yr	Per Wk Mo Yr 25 Yr
	Fry Trim	Fry Trim

Fry = Did you cook the game by frying it?

Trim = Did you remove the fat and skin from the game prior to cooking?

## OTHER ACTIVITIES AND HOBBIES

ID: [#1 #2 #3 #4 #5 #6 #7]

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Do you live alone? 1. YES 2. NO

If no, how many people are in your household?

In the last 10 years, have you or anyone else participated in any of the following activities in your house:

Activity	1=Yes 2=No	1=Self 2=Other 3=Both 8=NR 9=DK	# Times per Week (W), Month (M), Season (S), Year (Y), or 10 year period (10Y)	How many years in the last 10 yrs? u	How recently used?
Use paints, enamels, stains, sealers, or glazes for hobbies.	1 2	1 2 3 8 9	per W M S Y 10Y		
Use paints, enamels, stains, sealers, or glazes around the house.	1 2	1 2 3 8 9	per W M S Y 10Y		
Plumbing	1 2	1 2 3 8 9	per W M S Y 10Y		
Automotive or Farm/Lawn Equipment Repair	1 2	1 2 3 8 9	per W M S Y 10Y		
Welding/Metal Work/Soldering	1 2	1 2 3 8 9	per W M S Y 10Y		
Use glues, adhesives, or rubber cement at least once per month	1 2	1 2 3 8 9	per W M S Y 10Y		
Use mothballs in your closets or living space	1 2	1 2 3 8 9	per W M S Y 10Y	-	
Use silicone lubricants (like WD-40). Name of Compounds	1 2	1 2 3 8 9	per W M S Y 10Y		
Use chemical insect repellant (like OFF, Deet, etc.)	1 2	1 2 3 8 9	per W M S Y 10Y		
Used Pesticides, Insecticides, Herbicides at least once per month (Specify):	1 2	1 2 3 8 9	per W M S Y 10Y		
Target Shooting/Hunting	1 2	1 2 3 8 9	per W M S Y 10Y		
Other hobbies that use lead (e.g. stained glass) (Specify):	1 2	1 2 3 8 9	per W M S Y 10Y		
Other hobbies that use solvents (Specify):	1 2	1 2 3 8 9	per W M S Y 10Y		
Other hobbies that use other chemicals (Specify):	1 2	1 2 3 8 9	per W M S Y 10Y		

## FAMILY MEDICAL HISTORY

ID: [ #1 #2 #3 #4 #5 #6 #7 ]

Could you please tell me if your biological mother, father, sisters or brothers, or children were ever diagnosed with the following diseases?

				Biol	ogical Re	Biological Relative and approximate age of onset (99=DK)	mate age	of onset (99=DK)			
	Mother	er	Age	Father	Age	Sibling # 1	Age	Sibling # 2	Age	Child	Age
Alzheimer's or other dementia	1.Yes 2.No	No.		1.Yes 2.No		1.Yes 2.No		1.Yes 2.No		1.Yes 2.No	
2. No	8.NR 9. DK	DK		8.NR 9. DK		8.NR 9. DK		8.NR 9. DK		8.NR 9. DK	
Parkinson's Disease	1.Yes 2.No	.No		1.Yes 2.No	·	1.Yes 2.No		1.Yes 2.No		1.Yes 2.No	
2. No	8.NR 9. DK	. DK		8.NR 9. DK		8.NR 9. DK		8.NR 9. DK		8.NR 9. DK	
Multiple Sclerosis	1.Yes 2.No	No.		1.Yes 2.No		1.Yes 2.No		1.Yes 2.No		1.Yes 2.No	
2. No	8.NR 9. DK	. DK		8.NR 9. DK		8.NR 9. DK		8.NR 9. DK		8.NR 9. DK	

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I would like to ask you a couple of questions regarding your access to healthcare.

Do you currently have healthcare insurance? 1. Yes 2. No.

If yes: Is your healthcare covered privately, by an HMO or by Medicare/Medicaid?

How many years have you been covered by a healthcare plan?

GENERAL MEDICAL HISTORY				ID: [ #1 #2 #3 #4 #5 #6 #7 ]
Have you ever been told by a doctor that you had any of the following conditions?	he following condit	tions?		
Heart disease	2. No 1. Yes	8. NR	9. DK	If yes, Date of Diagnosis
Heart attack	2. No 1. Yes	8. NR	9. DK	If yes, Date of Diagnosis
High blood pressure	2. No 1. Yes	8. NR	9. DK	If yes, Date of Diagnosis
Emphysema	2. No 1. Yes	8. NR	9. DK	If yes, Date of Diagnosis
Asthma	2. No 1. Yes	8. NR	9. DK	If yes, Date of Diagnosis
Hay Fever	2. No 1. Yes	8. NR	9. DK	If yes, Date of Diagnosis
Auto-immune disorder (such as Lupus)	2. No 1. Yes	8. NR	9. DK	If yes, Specify Type(s)
				Date(s) of Diagnosis
Diabetes	2. No 1. Yes	8. NR	9. DK	If yes, Date of Diagnosis  Do you take insulin injections? No Yes
The control Discount of the	. No 1 Vac	QN 8	0 DK	If yes, What Type
Thyroid Disorders	2. NO 1. 103	0. MIN	2. DA	Date of Diagnosis
Arthritis	2. No 1. Yes	8. NR	9. DK	If yes, Date of Diagnosis
Carpal Tunnel Syndrome	2. No 1. Yes	8. NR	9. DK	If yes, Date of Diagnosis
Other Much or Ivint Condition	7 No. 1 Vec	an 8	את ס	If yes, What Type(s)
	Z. INO 1: 1C3	- 1	7. DA	Date(s) of Diagnosis

GENERAL MEDICAL HISTORY (continued)		D: [#1 #2 #3 #4 #5 #6 #7]
Have you ever been told by a doctor that you had any of the following conditions?	any of the following conditions?	
Gastrointestinal Ulcers	2. No 1. Yes 8. NR 9. DK	If yes, Date of Diagnosis
Kidney Disease	2. No 1. Yes 8. NR 9. DK	If yes, Date of Diagnosis
Bladder Disease	2. No 1. Yes 8. NR 9. DK	If yes, Date of Diagnosis
Liver Cirrhosis	2. No 1. Yes 8. NR 9. DK	If yes, Date of Diagnosis
Homotitic A/D/C/Othon	1	If yes, what type A B C Other
nepatius Av B/ C/ Ottlet	100 1, 163 0, 100	Date(s) of Diagnosis
	NO 1 Vag 8 ND 0 DV	If yes, What Type (s)
Cancer	NO 1. 165 6. IND	Date(s) of Diagnosis
Prostate Trouble (Men only)	2. No 1. Yes 8. NR 9. DK 0. NA	If yes, Date of Diagnosis
Abnormal Pap smear (Women only)	2. No 1. Yes 8. NR 9. DK 0. NA	If yes, Date of Diagnosis
Osteoporosis	2. No 1. Yes 8. NR 9. DK	If yes, Date of Diagnosis
Multiple Sclerosis	2. No 1. Yes 8. NR 9. DK	If yes, Date of Diagnosis
Stroke	2. No 1. Yes 8. NR 9. DK	If yes, Date of Diagnosis

GENERAL MEDICAL HISTORY (continued)		ID: [ #1 #2 #3 #4 #5 #6 #7 ]
Have you ever been told by a doctor that you had any of the following conditions?	ny of the following conditions?	
Parkinson's Disease	2. No 1. Yes 8. NR 9. DK	If yes, Date of Diagnosis
Severe Head Injury—	Act o can o can to can c	If yes, specify type
Loss of Consciousness of diagnosis of a concussion by a physician	2. NO 1. IES 8. NK 9. DA	Date of Diagnosis
A 12 hoisened, Diong on other Demonstin	o QN	If yes, specify type
Alzneimer's Disease or other Demenua	2. NO 1. ICS 0. NK 9. DA	Date of Diagnosis
A control Name of Control	AG 0 MB 0 DZ	If yes, specify type
Any Outer iveryous System Condition	0. INR	Date of Diagnosis
THE ALTERNATION	N. 1 V. C O NID	If yes, specify type
HIV/AIDS	2. NO 1. IES 6. NK 9. DK	Date of Diagnosis
Emotional Problems such as Clinical Depression or Anxiety Disorders	2. No 1. Yes 8. NR 9. DK	If yes, Date of Diagnosis
Ans. Other Health Condition	2 No. 1 Ver. 8 ND 9 DK	If yes, specify type
Any Onet meatur Condition	NO I. ICS COMIN	Date of Diagnosis
Horry vion loot woight in the last wan?	7 No 1 Vec 8 ND 0 DK	If yes, how many pounds?
nave you tost weight in the tast year?	NO I. IES	For what reason

### REPRODUCTIVE HISTORY (Women Only)

L# 9# ID: [ #1 #2 #3 #4 #5 The next part of the interview concerns your pregnancy history, including live births, stillbirths, tubal and other pregnancies, miscarriages, and voluntary terminations.

Have you ever been pregnant? 1. Yes

2. No 8. No Response

If yes: How many times have you been pregnant?

Have you ever had any difficulty becoming pregnant? 1. Yes

8. No Response 2. No Now I would like to obtain some detailed information about each of your pregnancies, starting with the first.

Preg #	Pregnancy Outcome	Date of Delivery or Loss (M/D/Y)	Was the child breast-fed?	If yes: For how many weeks?
	1. Livebirth 2. Twins 3. Miscarriage 4. Stillbirth 5. Voluntary Termination 6. Other 8.NR		1. Yes 2. No	
2	1. Livebirth 2. Twins 3. Miscarriage 4. Stillbirth 5. Voluntary Termination 6. Other 8.NR		1. Yes 2. No	
3	1. Livebirth 2. Twins 3. Miscarriage 4. Stillbirth 5. Voluntary Termination 6. Other 8.NR		1. Yes 2. No	
4	1. Livebirth 2. Twins 3. Miscarriage 4. Stillbirth 5. Voluntary Termination 6. Other 8.NR		1. Yes 2. No	
5	1. Livebirth 2. Twins 3. Miscarriage 4. Stillbirth 5. Voluntary Termination 6. Other 8.NR		1. Yes 2. No	
9	1. Livebirth 2. Twins 3. Miscarriage 4. Stillbirth 5. Voluntary Termination 6. Other 8.NR		1. Yes 2. No	
7	1. Livebirth 2. Twins 3. Miscarriage 4. Stillbirth 5. Voluntary Termination 6. Other 8.NR		1. Yes 2. No	
∞	1. Livebirth 2. Twins 3. Miscarriage 4. Stillbirth 5. Voluntary Termination 6. Other 8.NR		1. Yes 2. No	
6	1. Livebirth 2. Twins 3. Miscarriage 4. Stillbirth 5. Voluntary Termination 6. Other 8.NR	/_/_	1. Yes 2. No	
10	1. Livebirth 2. Twins 3. Miscarriage 4. Stillbirth 5. Voluntary Termination 6. Other 8.NR	/ /	1. Yes 2. No	

REPRODUCTIVE HISTORY (continued) Women Only)	D: [ #1 #2 #3 #4 #5 #6 #7 ]
fave your menstrual periods ceased permanently?No: Premenopausal	Yes: No menstrual periods
Yes: Had menopause but now have periods induced by hormones; age	Not sure
Vhat was your age at menopause?	
or which of the following reasons did your periods cease :	
a. Natural: 1. Yes 2. No	
If natural (non-surgical) menopause have you had subsequent surgery to remove your ovaries and/or uterus?	our ovaries and/or uterus?
NoOne ovary removedBoth ovaries removedU	Uterus removed Both uterus and ovaries removed
b. Surgery: 1. Yes 2. No	
If due to surgery, were your ovaries and/or uterus removed?	
One ovary removedBoth ovaries removedUterus removed	Both uterus and ovaries removed
c. Radiation or Chemotherapy? 1. Yes 2. No	
RadiationChemotherapy	

HEALTH HABITS  I would like to ask yo First, I'd like to know During the last 7 nigh Did you have trouble as physical and how stup physical activities. (has strenuous than brisk wator unming or jogging. Starting with mental activities (playing cards, board games, reading)	HEALTH HABITS  I would like to ask you some questions about your activity level during the past 7 days.  I would like to know a little about your sleep habits.  Enst, I'd like to know a little about your sleep habits.  During the last 7 nights, how many hours, on average, did you spend sleeping each night?  During the last 7 nights, how many hours, on average, did you spend sleeping each night?  Did you have trouble sleeping last night or the night before? ? 1. Yes 2. No 8. No Response  Did you have trouble sleeping last night or the night before? ? 1. Yes 2. No 8. No Response  Did you have trouble sleeping last night or the night before? ? 1. Yes 2. No 8. No Response  Did you have trouble sleeping last night or the night before? ? 1. Yes 2. No 8. No Response  Did you have trouble sleeping last night or the night before? ? 1. Yes 2. No 8. No Response  Did you have trouble sleeping last night of the night before? ? 1. Yes 2. No 8. No Response  Did you have trouble sleeping last night yells before? ? 1. Yes 2. No 8. No Response  Did you have trouble sleeping last night yells before? ? 1. Yes 2. No 8. No Response  Did you have trouble sleeping last night yells before? ? 1. Yes 2. No 8. No Response  Did you have considered moderage if they produce feelings similar or physical activities fall in between. People engage in many types of activities, and if you're not sure where your activities fit, please ask me. Starting with mental activities, please tell me what activities you did and for how many hours total during the week.  Specific Activity  Rouns activities (Plain activities and Plain activities fit has a first activities and activities and activities and activities and activities activities and activities activities activities and activities activitie	groups based on whether they are mental stivities to be light if they are less very hard if they produce feelings similar where your activities fit, please ask me.  Hours per Week
Light Physical Activities (less strenuous than brisk walking		

HEALTH HABITS (continued)	(continued)	#2 #3 #4 #5 #6 #7]
	Specific Activity	Hours per Week
Moderate		
Physical		
(similar to brisk		
walking)		
Hard		
Physical		
Activities (more than walking,		
less than jogging)		
Very Hard		
Physical		
(Similar to running		
or jogging)		
Compared to your n	Compared to your mental activity over the past year, was last week's mental activity (circle one): More	Less About the Same
Compared to your p	Compared to your physical activity over the past year, was last week's physical activity (circle one): More	re Less About the Same

HEALTH HABITS (continued)		

HEALTH HABITS (continued)	inued)		ID: [ #1 #2 #3 #4 #5 #6	[ 7# 9
I would like to ask you som	ne questions	I would like to ask you some questions about your use of tobacco and alcohol for the past 10 years.	oast 10 years.	
In the past 10 years, Did you:	1= Ever 2= Never	During the Past Year	In the Last 10 years	# of years in the last 10 years
Spend time in a location where you were <b>exposed</b> to second hand smoke at least once per week?	1 2	1. Yes avg. # hours  per day week month year  2. No 8. NR 9. DK	1. Yes avg. # hours  per day week month year 10 years 2. No 8. NR 9. DK	
Smoke <b>cigarettes?</b>	1 2	1. Yes avg. # per day week month year 2. No 8. NR 9. DK	1. Yes avg. #  per day week month year 10 years 2. No 8. NR 9. DK	
Smoke a <b>pipe?</b>	1 2	1. Yes avg. # bowls per day week month year 2. No 8. NR 9. DK	1. Yes avg. # bowls  per day week month year 10 years 2. No 8. NR 9. DK	
Smoke <b>cigars?</b>		1. Yes avg. #  per day week month year  2. No 8. NR 9. DK	1. Yes avg. #  per day week month year 10 years 2. No 8. NR 9. DK	
Use chewing tobacco?	1 2	1. Yes avg. # pinches  per day week month year  2. No 8. NR 9. DK	1. Yes avg. # pinches  per day week month year 10 years 2. No 8. NR 9. DK	

HEALTH HABITS (continued)	ned)		D: [ #1 #2 #3 #4 #5 #6 #7 ]	#7 ]
In the past 10 years, Did you:	1= Ever 2= Never	During the Past Year	In last 10 years	# of Years in the last 10 years
Drink beer/wine coolers?	1 2	1. Yes average # of 12 oz. cans, bottles, or glasses  per day week month year 2. No 8. NR 9. DK	1. Yes average # of 12 oz. cans, bottles, or glasses  per day week month year 10 years 2. No 8. NR 9. DK	
Drink wine?	1 2	1. Yes average # of 4 oz. glasses  per day week month year  2. No 8. NR 9. DK	1. Yes average # of 4 oz. glasses per day week month year 10 years 2. No 8. NR 9. DK	
Drink liquor or mixed drinks?	1 2	1. Yes average # of drinks with 1 ½ oz. of liquor per day week month year 2. No 8. NR 9. DK	1. Yes average # of drinks with 1 1/2 oz. of liquor  per day week month year 10 years 2. No 8. NR 9. DK	
Did was daint any alochalia havaranas in the last 21 hours?	The state of the s	a last 24 hours? 1 Ves 2 No 8 NR		

Did you drink any alcoholic beverages in the last 24 hours? 1. Yes 2. No 8. NR

2. Wine 3. Liquor or Mixed Drinks If yes: What did you drink? 1. Beer/Wine Coolers

How many drinks?

HEALTH HABITS (continued)	•		D: [#1	ID: [ #1 #2 #3 #4 #5 #6 #7 ]	2 #6 #7]
Have you taken any prescription or over-the-counter medications or supplements in the last 2 years?	cations or supplen	nents in the last 2	years? 1. Yes	2. No 8. NR	R 9. DK
[ IF YES, HAND	[ IF YES, HAND PARTICIPANT MEDICATIONS LIST]	MEDICATION	S LIST]	,	
Medication Name	Dose	Times per day	Use Now?	How Long?	Use in Last 24 hrs?
1)			`		·
2)					
3)			·		
4)					
5)					
(9)			,		-
()					
8)					
(6					
10)					
11)					
12)					

HEALTH HABITS (continued)			ID: [#1	#2 #3 #4	[ 2# 9# 5#
Medication Name	Dose	Times per day	Use Now?	e Now? How Long? Use in Last	Use in Last 24 hrs?
13)					
14)					
15)					
16)	:				
17)					
18)		,			
19)					
20)					
21)					
22)			•		
23)					
24)				·	

## Now I would like some information about your background:

Here is a card with a list of racial categories. Could you please choose one or more which describe your racial background:

- 2) Black or African American 1) White
- 4) Asian 3) American Indian or Alaska Native
- 5) Native Hawaiian or Other Pacific Islander
- 9) DK 8) NR
- Are you Latino or of Hispanic origin or descent? 1) Yes
- 8) NR 2) No
- 9) DK

Finally, please tell me which of the following categories includes your total family income before taxes:

- 8) Don't wish to answer
- 2) 15 to <30,000

1) <\$15,000

- 3) 30 to <45,000
- 4) 45 to <60,000
- 6) 60 to <75,000
- 6) >75,000

That concludes our interview. Do you have any questions?

Question:

Resolution:

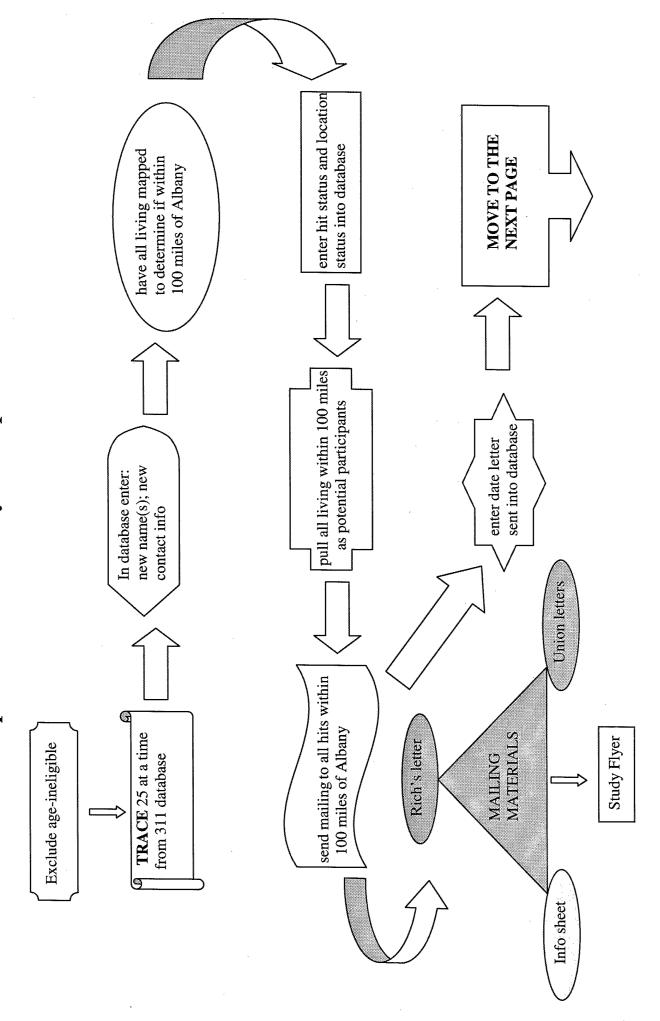
Thank you for your time and effort.

Interviewer's assessment of participant's thoughtfulness in	ipant's thought		responding to questionnaire (circle one):
1) Thoughtful, attentive to detail	2) Neutral	3) Superficial	3) Other (specify):
Problems during interview (circle all that apply):	all that apply):		
1) Difficulty understanding questions	s 2) Unsure of many	of many answers	3) Difficulty in concentration
4) Language difficulty 5) Emot	5) Emotionally distressed	d 6) Other (specify):	ecify):
If interviewer has any other comments, check here	ents, check here		and write them on back of this sheet.

### **APPENDIX 4**

Flow chart for tracing, screening and recruiting procedures for study subjects

# PCB Capacitor Worker Study Participant Recruitment Plan



(START)

Page 2 of 2

### **APPENDIX 5**

Informational material sent to prospective study participants

Wadsworth Center

The Governor Nelson A. Rockefeller Empire State Plaza

P.O. Box 509

Albany, New York 12201-0509

Antonia C. Novello, M.D., M.P.H., Dr. P.H. Commissioner

Dennis P. Whalen Executive Deputy Commissioner

DATE

NAME ADDRESS

Dear Mr./Ms\_\_\_\_\_

Staff from the New York State Department of Health (NYSDOH), in cooperation with Albany Medical Center and the University at Albany, are conducting a research study on the health effects of occupational exposure to polychlorinated biphenyls (PCBs) entitled 'Do PCBs Alter Dopamine Mediated Function in Aging Workers?' I am writing to you because, according to our records at the NYSDOH, you were employed at a factory where you may have been exposed to PCBs.

I would like to invite you to participate in this current research project that should improve our understanding of the neurological effects of being exposed to PCBs while at work. Your participation would entail completing an interview with the study coordinator, having blood drawn, completing a neurological assessment and having a test for bone lead content. Testing will take place at the Parkinson's Disease and Movement Disorders Center of Albany Medical Center on Washington Avenue Extension in Albany and at the NYSDOH in the Empire State Plaza in Albany. All testing will be conducted by qualified professionals free of charge to you. If you require assistance with travel to Albany, we will be glad to provide door to door transportation.

You will have the option of completing the tests in one full day in Albany, or splitting them into two partial days. For instance, the interview could be conducted a day or two earlier at a location in your community, and, if you wish, we will provide you with hotel accommodations in Albany the night before testing. Whichever option you choose, you will receive \$150 compensation for your participation, and travel expenses incurred will be reimbursed. Please refer to the enclosed question and answer sheet for more information.

Participation in this project is completely voluntary. Your decision whether or not to participate will not affect your relationship with any of your doctors or with Albany Medical Center.

Within the next week a member of my staff will telephone you to discuss your interest in this project. If you have any questions regarding this project, please feel free to call me toll-free at 866-852-2561.

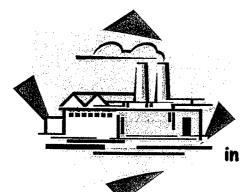
Thanking you in advance for your help, I remain,

Sincerely,

Richard F. Seegal, Ph.D.

Richard F. Seegol

Research Scientist and Principal Investigator



### The Capacitor Workers Study:

Do PCBs Alter Dopamine Mediated Function in Aging Workers?

If you worked at the Ft. Edward or Hudson Falls capacitor plants between 1946 and 1977, this is your chance to help us learn more about the neurological effects of PCBs.

Please consider participating in this important new health study.

You can earn at least \$150 dollars and contribute to our understanding of how PCBs affect the nervous system.

Dr. Rich Seegal and staff
NYS Department of Health
1-866-852-2561

### U.E. Local 332 145 Main Street Hudson falls, N.Y.



December 8, 2002

Dear Current and Former Members,

Dr. Richard Seegal, a Research Scientist at the New York State Department of Health in Albany, with support of UE Local 332, conducted a small pilot study to determine the long-range health effects that may be associated with occupational exposure to polychlorinated biphenyls (PCBs).

On Saturday, October 20, 2001 Dr. Seegal presented results from that pilot study and announced that he has received funds from the U.S. Army Medical Research Command to undertake a larger study of the potential health risks of occupational exposure to PCBs.

Former workers from the Fort Edward and Hudson Falls plants will be asked to participate in a one-day study to be conducted at Albany Medical Center. Participants will receive \$150 for their time and any travel expenses due to travel to and from Albany. In addition, some participants will be asked to travel to the Institute of Neurodegenerative Disorders in New Haven, CT in order to obtain brain images that will provide additional information concerning the effects of PCBs on the brain. This procedure will take two days and participants will receive an additional \$200 plus all travel expenses.

All procedures will be conducted under the supervision of a physician. They will include interviews and some simple tests of nervous system functions. A small blood sample will be drawn to measure the levels of PCBs in the blood and while in New Haven, a tracer dye will be administered by intravenous injection.

The Executive Board of UE Local 332 unanimously see this proposed research as a protection of our Members health as well as an important contribution to the general community. We urge you to participate.

Sincerely Yours;

Joyce Sumner, President

Robert Brown, Business Agent

Robert Brown

August 22, 2002

Dear Current or Former Member of UE Local 332,

I'm using this letterhead because it represents my relationship with many of you. What I need to say to you is of the greatest importance.

What it has to do with is your possible past exposure to PCBs at the GE mill - a subject of which you've heard plenty since 1975 - and the possibility of neurological, long-term consequences to that exposure. I can hear you saying, "We've been through all that. Why is this going on and on?" My answer to you is what Dr. Irving Selikoff said to me when he headed the "Mash type" massive investigation of GE workers 26 years ago, "Don't expect any quick answers on all of this PCB situation. I discovered the deadly effects of asbestosis decades ago but it took 40 years before the medical profession finally accepted it for what it is."

So the epidemiological study goes on - and one of the key factors as to whether the study will be successful is the rate of participation of eligible subjects.

In 1996 Dr. Richard Seegal, a personal friend for whom I have the highest regard, came with me to his first UE Local 332 Executive Board meeting. He was delighted to be talking to people who actually know about PCBs first hand, which certainly facilitated his suspicion that neurological consequences could eventually follow exposure. He has devoted a large chunk of his career to ascertaining the bottom line on all of this - maintaining episodic contact with our people over that time - and is now receiving funding to continue this important study entitled "PCBs Alter Dopamine-Mediated Function in Aging Workers."

I do most sincerely hope that you will find a way to cooperate with this study as fully as you can - not only for your own benefit but also to the benefit of other workers similarly effected and to the advance of medical knowledge generally. It isn't often that we get the opportunity to provide important witness to medical science.

With best wishes for your continuing health and well-being, I am

Sincerely and fraternally

Former UE International Rep.

### INFORMATION SHEET

### Do PCBs Alter Dopamine Mediated Function in Aging Workers?

October 2002

Prepared by staff of:

Wadsworth Center



### A Study of the Nervous System Related Health Effects of Occupational Exposure to PCBs

An epidemiological and clinical research study to determine the neurological and neuropsychological consequences of occupational exposure to polychlorinated biphenyls (PCBs) will be directed by staff of the Wadsworth Center of the New York State Department of Health. This project, supported by a grant from the United States Army Medical Research and Materiel Command, will involve multi-institution collaborations.

The goals of this research are to determine: (i) whether a relationship exists between serum PCB concentrations and/or duration of occupational exposure to PCBs and adverse nervous system health effects and (ii) if any adverse effects become more apparent in aging workers.

Participants will consist of male and female former capacitor workers who had been employed at the General Electric capacitor factories in Fort Edward and Hudson Falls, New York. Individuals will be identified from computer tapes listing all individuals who worked at either factory. Out of a total population of approximately 4,500 workers, 250 individuals will be studied; they must be currently at least fifty years of age and live within 100 miles of Albany. Initial contact will be by mail, with a subsequent telephone follow-up. At that time, a questionnaire will be administered that includes questions related to socio-economic factors, health habits and a short medical history. Institutional Review Board (IRB) approvals have been obtained from all participating institutions, including the United States Army Medical Research and Materiel Command.

Clinicians from the Parkinson's Disease and Movement Disorders Center of Albany Medical Center and the University at Albany will measure neurological and neuropsychological function. The neurological examination will measure nerve function, muscle strength, and reflexes. The neuropsychological examinations will include tests that measure muscle control, steadiness, memory and learning and whether participants are depressed. A non-invasive bone lead test will measure past exposure to lead. In addition, participants will be asked questions about where they have lived and worked, hobbies, general medical history, and health habits. Finally, a small amount of blood will be collected intravenously by a licensed phlebotomist in order to measure levels of PCBs. All tests will be administered and/or supervised by board-certified neurologists or neuropsychologists.

Analytical chemists at Mt. Sinai School of Medicine will analyze blood samples collected in Albany for concentrations of PCBs. These data will allow us to determine the relationship between the above described measures of nervous system function and PCB exposure.

Approximately 40% of the former capacitor workers who participate in the study in Albany will be selected, and asked, to participate in an additional study in New Haven, CT. Neurologists at the Institute of Neurodegenerative Disorders will investigate whether brain imaging with a radioactively labeled drug provides information concerning potential changes in neurotransmitter function due to occupational exposure to PCBs.

The project will begin in November 2002. It is anticipated that the interviewing, biological sampling and nervous system testing will be completed by December 2005, with a final report issued within a year of completion.





### Q. What is the primary goal of this project?

A. The primary goal is to determine if prior occupational exposure to PCBs increases the likelihood of neurological problems, including Parkinson's disease.

### Q. Why is this project important?

A. Studies of laboratory animals conducted by researchers at the New York State Department of Health's Wadsworth Center suggest that PCBs may cause biological changes in the nervous system. These changes may accelerate the effects of aging on memory, muscle coordination and control, and sense of smell. Understanding the relationship between previous occupational exposure to PCBs and possible changes in nervous system function may lead to better treatment of workers who have been exposed to high levels of PCBs or other toxic chemicals.

### Q. Who are the sponsors of the project?

A. The U.S. Army Medical Research and Materiel Command is funding this project. The study will be conducted by staff from the New York State Department of Health cooperation with Albany Medical Center and the University at Albany.

### Q. If I agree to participate, what will I be asked to do?

A. Your participation involves answering interview questions, having a blood sample taken to determine your blood PCB level, and undergoing non-invasive testing of various nervous system functions. These tests include a medical exam which takes approximately 60 minutes and tests of motor coordination and memory which will last approximately 2 1/2 hours. We will also estimate your past exposure to lead by non-invasively measuring your bone lead which takes approximately 30 minutes. All testing should take approximately 6 to 7 hours to complete.

In addition, a sub-group of participants will be asked to travel to New Haven, Connecticut at a later time for tests of brain imaging.

### Q. What is the schedule for testing?

A. You will be given the option to complete the testing in one full day in Albany, or to split the testing into two partial days. For instance, the interview could be conducted on the first day, in the afternoon, at a location either in your community or in Albany. The second day of testing, conducted in Albany, would then take approximately 5 hours to complete. If you prefer, overnight accommodations in an Albany area hotel will be provided.

### Q. What will the nervous system tests involve?

A. All nervous system tests are non-invasive and involve answering questions or identifying odors, shapes, colors and words, and performing simple tasks with your hands and fingers.

### Q. What kinds of questions will be asked during the interview?

A. The interview will include questions about residential, occupational and medical history. General questions will be asked regarding age, marital status, smoking history, alcohol consumption, diet, use of medications, and hobbies. The interview will last approximately 1 1/2 hours.

### Q. How much blood will be taken?

A. Ten milliliters or about two teaspoons of blood.

### Q. What is the purpose of the bone lead test?

A. The bone lead test allows us to estimate your past exposure to lead. We will use the results from this test to make sure that any relationship that we see between your nervous system test results and your PCB levels are not actually due to previous exposure to lead.

### Q. If I agree to participate, what are the possible risks?

A. Only a minor risk is involved for all of these procedures. Following the blood collection, some people may experience a small amount of bleeding, swelling, bruising or tenderness. The X-ray Fluorescence test is painless and involves exposure to only a very small amount of radiation, which is approximately 1/1000th of the exposure from a chest X-ray.

### Q. What does it mean if you find PCBs in my blood?

A. Most people have measurable levels of PCBs in their blood. However, because the measurement of PCBs in blood is not a standard clinical test we can not tell you what these results mean since the relationships between PCB exposure and nervous system function are not presently fully understood.

### Q. How will the project's results be used?

A. The results will be used to determine whether or not people with higher levels of PCBs score differently on tests of nervous system function than those with lower PCB levels.

### Q. Are all results confidential?

A. We will keep all research records that identify you confidential to the full extent allowed by law. However, someone from the Food and Drug Administration, Albany Medical College, the New York State Department of Health or the U.S. Army Medical Research and Materiel Command may inspect and/or copy the records that identify you as a part of their responsibility to protect human subjects in research.

### Q. Will I be compensated for my participation?

A. Your expenses for travel and meals will be reimbursed, and monetary compensation for the testing will also be provided.

### Q. Will I be I be informed of my test results?

A. You will not be informed of your test results, but you will be given the results of the research study. However, if a previously unknown neurological abnormality is found, your physician will be notified of this abnormality upon your authorization.

For more information about this project, please call Richard Seegal, New York State Department of Health, 1-866-852-2561 (toll free).

### ALBANY MEDICAL CENTER ALBANY, NY 12208

### PERMISSION TO TAKE PART IN A HUMAN RESEARCH STUDY

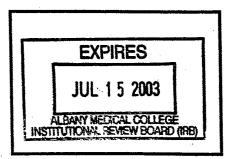
*Title of research study:* Do PCBs Alter Dopamine Mediated Function in Aging Workers?

**Principal Investigators:** Dr. Richard Seegal of the New York State Department of Health and Dr. Stewart Factor and of the Parkinson's Disease and Movement Disorders Center of Albany Medical Center

We invite you to take part in a research study because you may have been previously exposed to polychlorinated biphenyls (PCBs) at your job in either Fort Edward or Hudson Falls, New York. Your name and history of exposure to PCBs at work was obtained from records maintained by the New York State Department of Health from earlier research studies of PCB exposure in workers.

### What you should know about a research study

- We give you this consent form so that you can read about the purpose, risks and possible benefits of taking part in this research study. Please review it carefully.
- The main goal of regular medical care is to help each patient. The main goal of a research study is to learn things to help future patients.
- We cannot promise that this research study will help you.
- Just like regular medical care, your taking part in this research study can result in harmful effects that may be minor or serious.
- Someone will explain this research study to you. Feel free to ask all the questions you want before you make a decision.
- A research study is something you volunteer for. Whether or not you take part in this research study is up to you.
- You have the right to choose not to take part in the research study. Also if you agree to take part now, you can change your mind later on.
- Whatever you decide it will involve no penalty or loss of benefits that you would get anyway.



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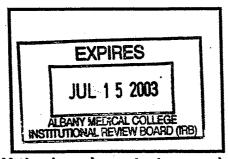
### 1 - Why is this research study being done and what is its purpose?

The purpose of this research is to determine if a relationship exists between PCB exposure and Parkinson's disease. This research is being done to study if neurological problems exist in people who had been exposed at their job to polychlorinated biphenyls (PCBs), a type of chemical used in factories to make electrical equipment. Understanding the relationships between previous exposure to PCBs at the work site and possible changes in nervous system function may lead to better treatment of workers who have been exposed to high levels of PCBs or other toxic chemicals, including lead which may cause neurological problems similar to those caused by PCBs.

This study will obtain measures of neurological function through physical tests and tests of memory and learning and relate these measures to PCB exposure in people who had been exposed at their job. We expect about 250 people will take part in the study, which will also include estimating lead exposure by measuring bone lead concentrations in your leg (shin) using a test similar to an X-ray. In addition, approximately 35% of the subjects will be chosen to participate in an additional portion of the study conducted at the Institute for Neurodegenerative Disorders in New Haven, CT. Selection will be based on the levels of PCBs in their blood. This portion of the study involves imaging brain function using very low levels of a radioactive compound ([123]CIT) and brain scans (Single Photon Emission Computed Tomography—SPECT). Subjects selected for this portion of the study will be given an invitation to participate and a description of the procedures to review prepared by neurologists at the Institute for Neurodegenerative Disorders. Please ask us if you have any questions regarding the purpose of this study.

### 2 - Who is doing the research study?

Dr. Richard Seegal, a Research Scientist at the New York State Department of Health and Dr. Stewart Factor, a Neurologist at the Parkinson's Disease and Movement Disorders Center of Albany Medical Center are the principal investigators. They, along with Dr. Eric Molho, a Neurologist at the Parkinson's Disease and Movement Disorders Center of Albany Medical Center, Dr. Robert McCaffrey, a Neuropsychologist in the Department of Psychology at the University of Albany, and Dr. Kenneth Marek, a Neurologist at the Institute for Neurodegenerative Disorders in New Haven, CT, are planning to conduct a research investigation. This research is supported by the U.S. Army Medical Research and Materiel Command.



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### 3 - What can you expect if you take part in this research study?

You will receive a physical examination that will take approximately 60 minutes. As part of this exam we will measure nerve function, muscle strength and reflexes. You will also be asked to get up from a chair and walk 50 feet in a straight line. You will also be asked to write a sentence and draw with each hand.

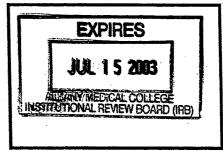
You will also receive tests that measure muscle control, steadiness, and measures of memory and learning. Finally, to learn whether you are feeling depressed or upset, a series of questions will be asked of you. These tests will take approximately 2 to 3 hours to complete.

You will also receive a test called X-Ray Fluorescence which takes a small X-ray of your shin bone to measure the amount of lead in that bone. You will be asked to sit quietly for about 30 minutes while this measurement is made.

We will ask you to complete an interview with a series of questionnaires that will take about one hour to complete. The interviewer will ask questions about where you have lived, where you have worked, your hobbies, your general medical history and your health habits. You have the right to not answer any question and can stop the interview at any time.

You will also be asked to provide a small sample of blood. This sample will be collected from a vein in your arm using a sterile needle, as in a routine blood test. Blood collection will take only a few minutes and will be collected at the Parkinson's Disease and Movement Disorders Center of Albany Medical Center under the supervision of Dr. Stewart Factor. The quantity of blood drawn will be 10cc (two teaspoons). This blood will be taken to measure PCBs and estimate your previous exposure to PCBs. We will also measure DDE, a marker of exposure to pesticides, and lipid levels which are used to report the PCB data. After these measurements have been made, the blood sample will be destroyed. All testing should take approximately 6 to 7 hours to complete.

You will be given the option to complete the testing in one full day in Albany, or to split the testing into two partial days. For instance, the interview could be conducted on the afternoon of the first day at a location either in your community or in Albany. The second day of testing, conducted in Albany, would then take approximately 5 hours to complete. If you prefer, overnight accommodations in an Albany area hotel will be provided.



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### 4 - What are the risks and possible discomforts?

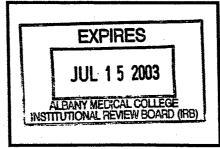
Only a minor risk is involved for all of these procedures. Following the blood collection, some people may experience a small amount of bleeding, swelling, "black and blue mark" or tenderness at the needle entry site. A risk of infection occurs rarely. Discomfort is minimal, resulting only from the initial needle prick. The X-Ray Fluorescence test is painless and involves exposure to only a very small amount of radiation which is approximately one-one thousandth of the exposure from a normal chest X-ray. There are no discomforts associated with the bone lead X-ray measurement and there are no side effects.

### 5 - What are the possible benefits?

A possible benefit to participating in this study is that knowledge obtained from the neurological and neuropsychological exams that are part of the research may uncover a previously unknown neurological abnormality. If found, your physician will be notified of this abnormality upon your authorization. Because the measurement of PCBs in blood is not a standard clinical test we can not tell you what these results mean since the relationships between PCB exposure and nervous system function are not presently fully understood. However, results from this study may ultimately aid in understanding the relationships between previous exposure to PCBs at the work site and possible changes in nervous system function.

### 6 - If you do not want to take part in the research study, are there other choices?

You are free to choose not to take part in this research study. Taking part in this study is voluntary. If you decide not to take part, there will be no penalty to you. You may also withdraw from the study at any time, without affecting or changing your medical care, by contacting Dr. Seegal toll free at 1-(866) 852-2561.



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### 7 - If you have any questions or problems, whom can you call?

If you have any questions about the research study now or later you should call Dr. Seegal toll free at 1-(866) 852-2561. If you think you have been injured by the research, you should call the study doctor, Dr. Factor, or an associate at (518) 452-0914. If you cannot reach them, or if you have any questions about your rights as a research subject, you may call the Albany Medical College, Office for Research at (518) 262-5182. For questions regarding the protection of human subjects call Tony Watson, Administrative Coordinator of the Institutional Review Board of the New York State Department of Health at (518) 474-8539.

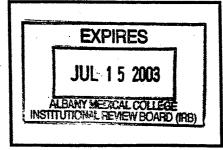
### 8 - What information will be kept private?

Efforts will be made to keep your personal information, including research and medical records, private. We can not guarantee absolute privacy. Organizations that may inspect and copy your private information include the Food and Drug Administration, the Department of Health and Human Services, the New York State Department of Health and Albany Medical Center. It should be noted that representatives of the U.S. Army Medical Research and Materiel Command are eligible to review research records as a part of their responsibility to protect human subjects in research.

No information will be released to anyone else unless authorized by you. Any information that specifically identifies you will be removed from the blood that is taken. The interview form will not have your name, street address or social security number on it. Results of the study may be published; however, your name will not appear in any report or publication.

### 9 - Can your taking part in the research end early?

You may decide not to continue in the research study at any time without it being held against you and without losing any benefits you currently have.



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### 10 - What else do you need to know?

You will not be allowed to access your research records.

This study will be carried out at no expense to you.

At the end of your visit to the Parkinson's Disease and Movement Disorders Center of Albany Medical Center you will receive \$150 for your time and will be reimbursed for travel expenses and meals that you may have paid for during your visit.

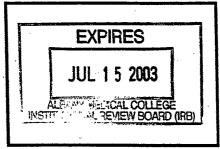
We will give you a signed and dated copy of this consent form.

You will not be informed of individual results, but will be given the results of the research study.

### Medical Care for Research Related Injury

The United States Department of Defense is funding this research project. Should you be injured as a direct result of participating in this research project, you will be provided medical care, at no cost to you, for that injury. You will not receive any injury compensation, only medical care. You should also understand that this is not a waiver or release of your legal rights. You should discuss this issue thoroughly with the principal investigator (Dr. Seegal) before you enroll in this study.

Other than medical care that may be provided and any other payment specifically stated in the consent form, there is no other compensation available for your participation in this research.



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### Do PCBs Alter Dopamine Mediated Function in Aging Workers?

Note: The subject must date the consent form at the time they sign it.

I have read the informed consent form and agree to participate in the research study described.

### **CONSENT OF RESEARCH SUBJECT**

Approval of research subject:	
Signature	Date Signed
Name (print or type)	
Street	▼ ···
City	State ZIP
Consent obtained by:	
Signature	Date Signed
Name (print or type)	
Title	
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EXPIRES

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INSTITUTIONAL REVIEW BOARD (IRB)

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### **APPENDIX 6**

Abstract and manuscript from presentation at New York Academy of Sciences conference titled: "Parkinson's Disease: The Life Cycle of the Dopamine Neuron", Princeton, NJ, September 18-20, 2002

Neurological Effects of Polychlorinated Biphenyls – Does Occupational Exposure Alter Dopamine-Mediated Function? R.F. Seegal<sup>1</sup>, K. Marek <sup>2</sup>, S. Factor <sup>3</sup>, R. McCaffrey<sup>4</sup>, R. Haase<sup>4</sup>, M. Wolff<sup>5</sup>. <sup>1</sup>Wadsworth Center, New York State Dept. of Health, Albany, NY; <sup>2</sup>Institute for Neurodegenerative Disorders, New Haven, CT; <sup>3</sup>Albany Medical Center, Albany, NY; <sup>4</sup>University at Albany, Albany, NY, and <sup>5</sup>Mount Sinai School of Medicine, New York, NY.

Exposure of capacitor workers to polychlorinated biphenyls (PCBs) resulted in serum levels 100-fold higher than in unexposed individuals. These levels may well be of concern since exposure of adult non-human primates to PCBs, resulting in comparable serum levels, reduced basal ganglia dopamine (DA) concentrations and the number of tyrosine hydroxylase positive neurons in the substantia nigra-even after exposure to PCBs ceased. Based on these data we conducted a pilot study of former capacitor workers and age-and gender-matched controls in which we measured neurological and neuropsychological performance and serum PCB levels. Former workers had: (i) longer reaction times and performed less well on measures of motor function and memory; (ii) higher scores on Part III of the Unified Parkinson's Disease Rating Scale; (iii) greater tremor, rigidity and bradykinesia and (iv) higher serum PCB levels. We are now undertaking a larger and more comprehensive study of former capacitor workers. In addition to the above measures, we will also determine basal ganglia DA transporter densities, using β-CIT SPECT imaging, and bone lead concentrations using X-Ray fluoresence. These studies will determine whether: (i) PCBs alter DA terminal densities; (ii) reductions in DA terminal densities influence neurological function and (iii) elevated lead interacts with PCBs and influences neurological outcomes. These studies should also provide insights on the consequences and mechanisms of action of structurally and/or toxicologically similar contaminants (e.g., dioxins and furans) on human DA function. Supported by the US Army Medical Research and Materiel Command.

Neurological Effects of Polychlorinated Biphenyls – Does Occupational Exposure Alter Dopamine-Mediated Function?

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Running Title: PCBs and Dopamine Function

Key Words: polychlorinated biphenyls, occupational exposure, dopamine, neurological function

Polychlorinated biphenyls (PCBs), once heavily used in industry, are now widespread environmental contaminants, which have been suggested to be associated with developmental and cognitive deficits in infants and children born to mothers who consumed food products contaminated with PCBs and other toxicants. These data, supported by studies of laboratory animals exposed during development to PCBs, as reviewed by Seegal, suggest that the developing central nervous system (CNS) is sensitive to this toxicant. However, both *in vitro* and *in vivo* data described below suggest that: (i) susceptibility extends beyond the perinatal period, and (ii) PCBs induce long-term alterations in dopamine (DA) function, including reductions in *de novo* synthesis and inhibition of monoamine transporter function. These findings, in turn, provide a biologically based rationale for examining neurological function in a cohort of aging former capacitor workers who had been exposed to extraordinarily high levels of PCBs.

### PCBs ALTER DOPAMINE FUNCTION IN VITRO

PCBs reduce DA content in tissues derived from laboratory rodents, including pheochromocytoma (PC12) cells, adult striatal tissue and synaptosomes exposed *ex vivo* to PCBs, and they elevate media DA concentrations.<sup>3</sup> These changes in DA function may, in part, involve PCB-induced inhibition of monoamine transporters, including the membrane dopamine transporter (DAT) and the intra-cellular vesicular monoamine transporter (VMAT).<sup>4,5</sup> The consequences of such transporter inhibition include increased free cytosolic DA, elevations in both tissue and media concentrations of 3,4-dihydroxyphenylacetic acid (DOPAC), and enhanced formation of DA quinones and semi-quinones, leading to generation of hydrogen peroxide and other reactive oxygen species.<sup>6</sup>

### PCBs ALTER DOPAMINE FUNCTION IN VIVO

The alterations in DA function described above may explain the neurochemical and neuropathological consequences of long-term exposure of the adult non-human primate (NHP) to PCBs. Thus, in adult NHPs exposed to PCBs for 20 weeks, an exposure that results in serum concentrations similar to those seen in former workers, basal ganglia DA concentrations were significantly reduced. Furthermore, when additional NHPs were exposed to similar levels of PCBs, but were then removed from exposure for

24 or 44 weeks prior to sacrifice, brain DA concentrations remained depressed, and were not significantly different from DA levels in NHPs sacrificed during exposure, despite dramatic reductions in serum PCB levels (Fig. 1). This pattern suggests long-term, if not permanent, changes in DA function. A likely explanation for these persistent reductions in basal ganglia DA concentrations is based on our findings that the number of TH+ neurons in the NHP substantia nigra pars compacta was reduced by approximately 50% (Fig. 2).

These laboratory findings, incorporating both *in vitro* and *in vivo* techniques, provide compelling evidence that PCBs alter central DA function, including inhibition of monoamine transporter function, leading to premature death of central DA neurons. When combined with the above-described studies in NHPs, the primarily *in vitro* studies suggest that high-level (*e.g.*, occupational) exposure of adults to PCBs may have long-term consequences on DA-mediated function, including possible deficits in cognition and motor control. We have an opportunity to test that hypothesis in an aging cohort of former workers, who have been exposed to PCBs at concentrations so high that serum levels, measured 3 years after exposure ceased, were at least 100-fold higher than in non-occupationally exposed individuals. Neurological and neuropsychological examinations of these workers will allow us to determine: (i) the relationships between PCB body burdens and observable dysfunctions, and (ii) whether pathology similar to that seen in adult NHPs exposed to PCBs also occurs in aging former capacitor workers as determined by SPECT  $\beta$ -CIT imaging of basal ganglia DAT.

### REFERENCES

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### Aroclor 1016 (20-week exposure (3.2 mg/kg/day))

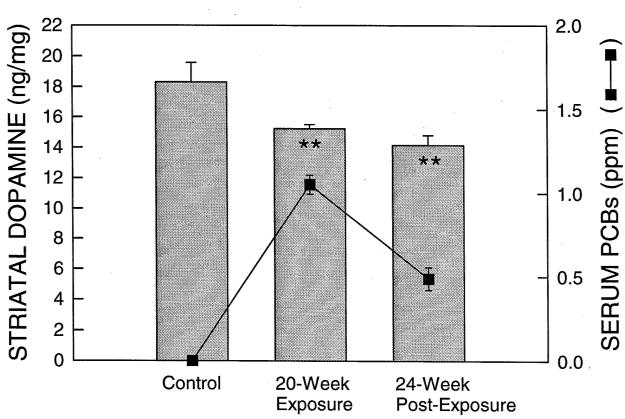
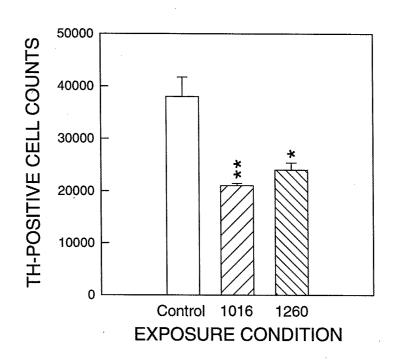


FIGURE 1. Striatal dopamine and serum PCB concentrations in non-human primates (macaques, Macaca nemestrina) exposed as adults to PCBs and sacrificed either immediately or 24 weeks following exposure. \*\*= $p \le 0.01$  compared to controls; N=3-5 animals per exposure condition.



**FIGURE 2.** Tyrosine hydroxylase (TH)-positive cell counts in the substantia nigra of non-human primates exposed to  $3.2 \,\text{mg/kg/day}$  of PCBs for 66 weeks before sacrifice. \*= $p \le 0.05$ , \*\*= $p \le 0.01$  compared to controls; N=3 animals per exposure condition.